

Gonorrhea

The Office Management of Acute Infections

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■ *Gonorrhea has recently increased to epidemic proportions and is poorly controlled. The principal causes are probably increasing resistance of *Neisseria gonorrhoeae* to penicillin, the difficulty of establishing the diagnosis and proving the cure in female patients and the inadequacy of resources devoted to the eradication of the disease by public health agencies.*

While examination of smears is adequate for diagnosis of the disease in males, in females cultures of vaginal exudate are necessary. Gonorrhea can usually be successfully treated with large doses of short-acting penicillins. Intramuscular administration of aqueous procaine penicillin will bring about cure in most cases. Female patients should have cultures for several weeks to make sure they are cured.

The physician should report all cases to the local health department so that contacts can be traced and treated.

OVER THE PAST DECADE reported gonorrhea in California increased from 16,021 cases in 1954 to 35,665 in 1964. The experience was similar throughout the nation and indeed in many parts of the world.² To date there are no signs of a reversal of this trend.

The reasons for this epidemic do not seem to be well understood, but related factors are the difficulty of diagnosing infections in females (probably the main reservoir of the disease) and of demonstrating cure by bacteriological techniques.³ Often in the clinic of the Berkeley City Health Department, females examined because of gonorrheal contact are found to be completely asymptomatic, yet a culture of vaginal exudate grows *Neisseria gonorrhoeae*. Rectal gonorrhea in males is also usually completely asymptomatic and is only detected by routine cultures. An occasional

male appears to be a urethral "carrier,"⁴ having very minor symptoms which one would be inclined to ignore, yet culture of material from the urethral meatus will grow the organism.

Other factors in the epidemic are that the gonococcus has an ability to mutate and to adapt to antibiotics; the incubation period is short and the disease is readily transmittable on mucous membrane contact; there is poor reporting of the disease by physicians; and in many health departments resources for doing the necessary contact tracing are inadequate. Moreover, so rapid have been the changes in therapy that many practitioners are confused about the correct procedure and are unaware of the concept of "epidemiological treatment."

Diagnosis

Typically in men the incubation period for gonorrhea is three to seven days and the first symptoms are dysuria and a thick pus-like urethral

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discharge. On occasions, symptoms may be much milder and the discharge may be scant. It is desirable to confirm the clinical impression by examination of a smear. A methylene blue smear is easily prepared and examined in the office as described later.

A word of caution: It is easy to diagnose typical male gonococcal urethritis but the less typical cases should not be dismissed as nonspecific urethritis unless a properly taken culture shows no growth of the organism.

In the case of male homosexuals or women who have had rectal exposure, a culture is taken of material obtained by introducing the swab into the anal canal.

For males with a typical urethral discharge, smears alone will suffice to determine the diagnosis, and cultures are not necessary. However, in the case of a male with symptoms so slight that the diagnosis might well be nonspecific urethritis, a culture should be made. Cultures of material taken from the urethral meatus of the male will sometimes be positive even though no discharge is visible.

In summary, gonorrhea in males can be confirmed by smears but should not be excluded without cultures.

In women, acute gonorrhea may be completely asymptomatic or the patient may complain of urinary symptoms, vaginal discharge or lower abdominal pains. The complications in women are extensive and may include the whole gamut of pelvic inflammatory disease.

Throughout the whole course of disease, diagnosis in women is difficult and demonstration of the gonococcus by laboratory methods is inconsistent. On physical examination, the finding of vaginal discharge is of very little help since clinically this cannot reliably be differentiated from discharge associated with trichomoniasis, moniliasis or nonspecific vaginitis. However, if pus is pressed out on stripping the urethra or involvement of Bartholin's gland is noted or pain is evoked on moving the cervix, gonorrhea should be suspected.

Smears of vaginal discharge are of no great help as the miscellany of organisms makes the identification of gonorrhea difficult. However, properly taken cultures are valuable.

Differentiation from Nonspecific Urethritis

Nonspecific urethritis is a symptom of many diseases, not a single disease entity. It may or may

not be associated with intercourse, and the incubation period is highly variable and usually prolonged, as distinguished from the usual two to three days for gonococcal urethritis in males. The discharge tends to be scant, white and mucoid. The smear shows miscellaneous organisms, on culture there is no growth of *Neisseria gonorrhoeae* and the response to treatment is disappointing.

Smears

A smear of the discharge should be lightly spread on a microscope slide.

If the specimen is examined in a well-equipped laboratory, it will be Gram-stained and the examiner will look for Gram-negative intracellular diplococci.

In the office, a smear can be prepared by placing a drop of methylene blue on the slide, immediately washing it off under the tap and drying the slide over a lamp. The specimen is then examined under the oil immersion lens, and the intracellular diplococci are easily seen. In the Berkeley clinic we have found methylene blue smears helpful in confirming the clinical impression of gonorrhea and in differentiating it from nonspecific urethritis. However, it should be recognized that this method is not completely specific, as it will not differentiate Gram-positive and Gram-negative organisms.

Cultures

Material for cultures must be collected with special equipment. For this purpose the State Department of Public Health laboratory provides special charcoal-impregnated swabs and mailing tubes of Stuart's transport medium, which is an anaerobic medium. Different laboratories throughout the state will provide slightly different kits.

It must be noted that specimens collected on an ordinary sterile swab and introduced into a dry sterile tube are not satisfactory.

In females, one culture should be taken from the cervical os and one from the urethra. Both swabs can be introduced into the same tube of transport medium.

Treatment

Antibiotics

A great deal of confusion surrounds the use of antibiotics because treatment has changed over the years.

When sulfonamides became available in the 1930's, the gonococcus was found to be susceptible and at first the results of treatment were good. However, within a few years many strains of gon-

ococcus developed resistance to the sulfa drugs. Today sulfonamides are not usually effective in the treatment of gonorrhea and use of them should be avoided.⁵

With the introduction of penicillin in the 1940's, a rather similar cycle of events occurred. At first very small amounts of penicillin killed almost all strains of gonococcus, but over the years many strains showed increasing resistance. However, this resistance to penicillin is relative: The gonococcus remains susceptible to penicillin in higher doses, and penicillin of the right type in the right dose continues to be the drug of choice for the treatment of gonorrhea.

The essential point is that the amount of penicillin required to cure gonorrhea has gradually increased over the years and many customary treatment schedules are no longer effective.⁵

Types of Penicillin

There is an unfortunate tendency to talk of penicillin as though it were a specific drug. It is not. There are many different types of penicillin with different pharmacological properties and different indications for use. The following three basic types of penicillin are used in venereal disease clinics.

Aqueous procaine penicillin G (APP.) A short-acting preparation which rapidly attains high levels in the blood and is eliminated from the body in about 24 hours.

Procaine penicillin G with 2 per cent aluminum monostearate (PAM.) This preparation is released into the bloodstream more slowly than APP, does not reach blood levels as high as those with APP and persists in the body for 24 to 72 hours.

Benzathine penicillin G. This is the longest acting of the penicillins. It is released slowly into the blood, the blood levels are relatively low and it persists in the body for about one month.³

Gonorrhea is best treated with high blood levels of penicillin, which need be present only for a short time. Hence APP or combinations of APP and PAM are suitable. APP alone in high doses is the best treatment for gonorrhea and it is particularly suitable for resistant cases.¹ The combination of APP and PAM is more likely to eradicate concurrently acquired syphilis and is, therefore, the logical choice for the routine treatment of gonorrhea.

In most venereal disease clinics benzathine penicillin is considered to be contraindicated in the

treatment of gonorrhea because the prolonged low level penicillinemia is conducive to the development of resistant gonococcal strains.⁵ It should never be used alone in the treatment of gonorrhea. Benzathine penicillin is, however, the drug of choice for the treatment of syphilis.

Recommended Treatment

In Berkeley City Health Department's Venereal Disease Clinic the following treatment has been used for some years with a low failure rate, probably 1 or 2 per cent.

FOR UNCOMPLICATED GONORRHEA

Male Urethritis	} APP* and PAM* 1.2 million units (MU) intramuscularly of each
Female Urethritis, Cervicitis	
Epidemiological Treatment of	
Female Contacts	

The USPHS has recently been advocating the use of twice the above dose (namely 2.4 MU each of APP and PAM⁶). However, it is difficult to administer that much penicillin to a patient, and the cure rate with 1.2 MU of each intramuscularly appears to be continuing at a satisfactory level.

For Resistant Gonorrhea

Resistant gonorrhea should be treated by doubling the original dose of antibiotics. In the Berkeley clinic, the intramuscular dose is increased to 2.4 MU each of APP and PAM and this treatment is invariably successful. The treatment of the complications of gonorrhea such as pelvic inflammatory disease and septic arthritis is beyond the scope of this article, except to mention that treatment is individualized and large doses of short-acting penicillin are used.

Allergic Sensitivity to Penicillin

Patients who have allergic sensitivity to penicillin can be treated with tetracycline USP capsules: One gram to begin with, then 0.5 gram every six hours for four days (36 capsules).

Follow-up of the Female Gonorrhea Patient

After the initial treatment females should be seen weekly, cultures being made each time of material taken from the urethra and cervix until successive cultures show no growth of organisms. If cultures continue positive, either reinfection or resistant gonorrhea is the cause.

*APP=aqueous procaine penicillin G; PAM=procaine penicillin G with 2 per cent aluminum monostearate. These penicillins are commonly available as:

Aqueous Procaine Penicillin G—*Crysticillin*® (Squibb); *Wycillin*, (Wyeth); *Duracillin*® (Lilly); *Abbecillin*® (Abbott); *Biurnal-Penicillin*® (Upjohn).

Procaine Penicillin G with 2 per cent aluminum monostearate—*Crysticillin P.A.M.*® (Squibb); *Depo-penicillin*® (Upjohn); *Leptopen*® (Wyeth); *Duracillin-in-oil*® (Lilly).

Reinfection is treated with the same dosage as the original illness. Resistant gonorrhea is treated with double the original dose of antibiotics administered at one time. For the rare patient with repeatedly positive cultures, we have treated successfully with APP, 4.8 MU intramuscularly, repeated two days later.

In the female patient, proof of cure is difficult to obtain by laboratory methods, yet the inadequately treated female who becomes an asymptomatic carrier is a major factor in the spread of the disease. Hence, the patient should not be considered cured until two or three successive cultures have been negative.

Treatment of Nonspecific Urethritis

Prostatic massage is frequently employed in treatment of nonspecific urethritis although most textbooks hold it valueless as a therapeutic measure. Tetracycline is usually given in therapeutic doses. A mild discharge which clears spontaneously or after a few days of tetracycline, is probably of little consequence, but a more persistent discharge warrants referral to a urologist.⁴ Most nonspecific urethritis responds to a course of tetracycline USP 250 milligrams four times a day, for four to six days.

Epidemiological Treatment

Since gonorrhea in women is frequently asymptomatic and demonstration of the gonococcus by laboratory methods is inconsistent,⁵ the USPHS recommends treatment of any female who is identified as a contact of a male who has the disease. This "epidemiological treatment"—which is the same as for uncomplicated acute gonorrhea—is standard practice in most venereal disease clinics. The purpose is to eradicate the carrier state in the woman and to prevent the progression of illness.

Differentiation of Reinfection and Drug Resistance

If gonorrheal reinfection is suspected, it should be treated as a new case. On the other hand, if drug resistance is suspected, double the original dose of antibiotics should be given at one time. The differentiation of these two conditions is based primarily on the history obtained from the patient and may well tax the physician's diagnostic acumen, not to speak of his credulity.

Concurrently Acquired Syphilis

Syphilis and gonorrhea are both transmitted by sexual intercourse and often a patient with

gonorrhea will have a positive reaction for syphilis by the Venereal Disease Research Laboratory (VDRL) test.

The dosages of aqueous procaine penicillin G and procaine penicillin G with 2 per cent aluminum monostearate recommended for gonorrhea will probably abort concurrently acquired syphilis. Nevertheless, any patient with a positive result of VDRL test (which is not reported until after the treatment for gonorrhea has been given) should be seen again and his condition assessed in the light of this new finding.

It should be borne in mind, however, that the recommended dosage of tetracycline for patients who have allergic sensitivity to penicillin is definitely inadequate to abort syphilis. Therefore, patients treated with tetracycline should have a serologic test for syphilis at the time of treatment and again several months later.

Reporting to the Health Department

Most males with gonorrhea will seek treatment for themselves, but their female contacts are usually unaware of the disease. Not only are they a reservoir for the spread of gonorrhea, but delay in treatment until they become symptomatic may well result in irreversible pathological changes. Similarly, the homosexual male with rectal gonorrhea is usually asymptomatic and constitutes another reservoir of the disease. Most health departments have trained venereal disease investigators who can help physicians to bring these contacts to treatment. California law requires that physicians report any cases of venereal disease to the local health department.

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